Remarks

Claims 1-20 were pending in the application. Claims 6-8, 14-16 and 20-22 stand withdrawn from consideration as a non-elected invention under the restriction requirement. Claims 16, 17 and 18 are cancelled herein.

Claims 1, 9, 10 and 11 are currently amended. Support for the amendments is found throughout the specification and claims as originally filed. Specifically, support for the added language "administering a cad-11 antisense or sense oligonucleotide" is found at page 6, lines 10-14, lines 16-19, lines 21-25, page 9, lines 19-21 and page 10, lines 1-7 and 28-31. It is clear from the specification that an "agent" that interferes with cad-11 expression was meant to include methods of preventing translation and transcription of cad-11 through the use of cad-11 antisense and sense oligonucleotides. Furthermore, the specification teaches that DNA encoding a cad-11 polypeptide <u>is</u> useful for the production of such oligonucleotides and that nucleotides could be delivered or administered in an effort to contact cells. Specifically exemplified antisense molecules OB-1 SEQ ID NO:1 and OB-2 SEQ ID NO:2 are shown at page 22 and were selected from a full length cad-11 cDNA sequence as described at page 22 (lines 11-16).

Claims 21-24 are new. New claim 21 finds support at page 4, lines 5-9 and page 22, lines 11-19. New claims 22-24 find support at page 9, lines 1-3 and 19-21.

The sequence listing has been amended to respectively include as SEQ ID NOs: 5 and 6, the polynucleotide and amino acid sequences, SEQ ID NOs: 57 and 58, of cad-11 set out in United States Patent No. 5,597,725 issued January 28, 1997. The patent is incorporated by reference at page 4, line 7-8 of the present application and the addition of these sequences to the sequence listing does not add new matter. A statement under 37 C.F.R. §1.821(f) is submitted herewith. The specification has been amended at pages 4 and 22 to refer to SEQ ID NO: 5.

The Rejections under 35 U.S.C. § 112, First Paragraph
<u>(Written Description) May Be Withdrawn</u>

Claims 1-5, 9-13 and 17-19 are rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification purportedly does not provide an adequate written description of the claimed invention.

Applicant respectfully submits that the claims as presently amended comply with the written description requirement. For example, currently amended claim 1 is directed to cad-11 antisense or sense oligonucleotides derived from a cad-11 sequence. Cad-11 sequences were known in the art when the application was filed as is described at pages 4-5 of the specification and would be apparent to persons of skill in the art. In any case, the sequence listing of the application is amended herein to include the cad-11 DNA and amino acid sequences from United States Patent No. 5,597,725 that was incorporated by reference in the application as filed.

The present application provides a method of modulating differentiation or neoplastic transformation of cells. The instant application includes working examples (SEQ ID NO:1 and SEQ ID NO:2) of antisense oligonucleotides that bind and inhibit cad-11 cells in culture (p. 23 lines 5-11), inhibit cellular differentiation and fusion and reduce cell viability (p. 25 lines 17-30). Applicant respectfully submits that the specification further provides an appropriate written description which teaches methods for synthesising oligonucleotides at page 9, methods for delivering antisense oligonucleotides to cells at pages 10-11 and furthermore describes a method by which potential antisense or sense oligonucleotides could be selected (p. 22 lines 11-19) and tested in cell culture assays (at pages 22-26). Furthermore, the present specification specifically teaches methods for identifying antisense oligonucleotides from a cad-11 sequences generally and more specifically from SEQ ID NO:5. Such sense or antisense sequences are generally short in the range of 7 to 50 bases but preferably between 13 to 20 bases (page 9, line 1). The specification also teaches that such

short DNA or RNA molecules made with a sequence which is intended to be complementary to "unique" sequences in a gene or mRNA for a particular protein are useful in interfering with translation and transcription of nucleic acids for the protein (or sequences of low homology to other sequences - page 22 ,line 15).

A person of ordinary skill in the art would be able to immediately recognize the possible sense and antisense oligonucleotides which could be derived from a cad-11 sequence and further test candidate sequences as taught in the instant application. Thus there is no question that the specification as filed provides a written description of the claimed fragments.

The Examiner cites *The University of California v. Eli Lilly and Company* 43 USPQ2d 1398 (CAFC, July 1997) in support of the rejection for lack of written description. Applicant respectfully submits that facts underlying the Eli Lilly decision are different from those herein. In *Eli Lilly*, the Court held that disclosure of rat insulin encoding cDNA does not provide adequate written description of claims generically reciting cDNA encoding vertebrate insulin or mammalian insulin. The single species of vertebrate or mammalian cDNA disclosed did not describe the entire genus of vertebrate or mammalian cDNAs claimed. The instant case is very different. Cadherin-11 DNA sequences were known in the art when the present application was filed. It is from these known sequences, rather than from unknown sequences as in *Eli Lilly*, that sense or antisense oligonucleotides are selected as taught by the present invention. A skilled person can visualize or recognize the identity of the oligonucleotides recited in the claims.

The Examiner also suggests that the effective antisense nucleotides would be difficult to predict and further suggests that this unpredictability is related to accessibility of antisense molecules to their respective complementary sites (Examiner is relying on Branch TIBS Vol. 23, February 1998). Applicant respectfully submits that unpredictability in the art is not a sufficient reason to support a rejection for lack of adequate written description (Manual of

Patent Examining Procedure 2163 at page 2100-170 III(a), second last paragraph, right hand column). Branch admits (first page, far right column, bottom) "both oligodeoxynucleotides (ODNs) and bioengineered ribozymes can undeniably hit their intended targets." Moreover, as is discussed below, the present application is enabling.

Applicant therefore submits that the lack of written description rejection of claims 1-5, 9-13 and 17-19 under 35 U.S.C. § 112 , first paragraph, may be withdrawn.

The Rejection under 35 U.S.C. § 112, First Paragraph
<u>(Enablement), May Properly Be Withdrawn</u>

The Examiner has rejected claims 1-5, 9-13 and 17-19 under 35 U.S.C. § 112, first paragraph for purportedly failing to comply with the enablement requirement. The Examiner acknowledges that the specification provides general guidance for the methods of the invention, but asserts that the specification does not provide "any specificity in the practice of the claimed methods" (Action page 7, first paragraph, last sentence). The Examiner contends that antisense therapy is "an unpredictable art where specific guidance in the antisense sequence and modes of delivery of antisense oligonucleotides for any particular treatment (a specific cancer for example) is needed". With respect to the assertion that undue experimentation is required to practice antisense therapy according to the methods of the invention, the Examiner relies on a number of references to assert that the field of antisense therapy is unpredictable. Applicant respectfully submits that such a statement is tantamount to stating that any claim pertaining to antisense therapy is automatically in a suspect field and that, absent proof of a completely reliable cures in human patients, there can be no patents in the field of antisense therapy.

The standard for enablement requires that the specification be enabling to a person "skilled in the art to which it pertains and with which it is most nearly connected." (MPEP Section 2164.05(b)). The level of skill in the art of antisense therapy is generally high and

even if the applicant was to agree with the Examiner's assertions that some experimentation may be required to practice the invention as claimed, applicant submits that any such experimentation is not undue or unreasonable, which is the applicable standard (MPEP Section 2164.01). Even complex experimentation, involving an extended period of time and expense, is not necessarily undue if the experimentation is routine and the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (MPEP Sections 2164.01 and 2164.06). In the present case, the novelty of the present invention lies, in part, in the use of the claimed oligonucleotides to modulate differentiation or neoplastic transformation of cells. The delivery of antisense oligonucleotides is discussed at pages 10 and 11 of the specification. Furthermore, the preparation of appropriate oligonucleotides is discussed at page 9 (lines 1-31) and at page 22 (lines 11-26). In addition, the specification teaches methods for testing candidate oligonucleotides at pages 23-26. Thus, the specification provides sufficient guidance to enable a skilled person to practice the methods of the invention in antisense therapy techniques, and this guidance is not negated by assertions that antisense therapy is an emerging technology.

Applicant therefore submits that the lack of enablement rejection of claims 1-5, 9-13 and 17-19 under 35 U.S.C. § 112 , first paragraph, may be withdrawn.

The Rejection under 35 U.S.C. § 101 May Be Withdrawn

The rejection may be withdrawn as claims 16-19 are cancelled herein.

Priority Claim

Applicant submitted by express mail on November 23, 2003, a petition for acceptance of an unintentionally delayed claim for priority under 35 U.S.C. §119(e)(1) and §365(c). The petition included an amendment inserting a priority reference in the present application.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant submits the application is in condition for allowance and early notice of the same is respectfully requested.

Respectfully submitted,

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